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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/083,058	02/25/2002	Svend Havelund	5386.224-US	6987

7590 05/27/2004

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EXAMINER	
GUPTA, ANISH	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 05/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/083,058	HAVELUND ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 61-69 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 61-69 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed 2-25-02 is acknowledged. Claims 1-60 were cancelled and claims 61-69 were added. Claims 61-69 are pending in this application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

1. Claims 61-69 are rejected under 35 U.S.C. 102(e) as being anticipated by Havelund et al.

The claims are drawn to water soluble aggregate of an insulin derivative having a lipophilic group and has a molecular weight larger than aldolase and comprise at lease 2 zinc ions per 6 moles of insulin derivative.

The reference teach a composition comprising 600 nmol/ml of Lys B29-Nε-(hexadecanoyl)-insulin, 7 mM of sodium phosphate buffer at pH 7.5, 10 mM sodium chloride, 16 mM phenol, 16 mM cresol, 2-3 Zn+2/hexamer and 1.6%(w/v) glycerol (see col. 32, lines 34-48). The reference also discloses similar pharmaceutical formulations for Lys B29-Nε lithocholyl human insulin (see col. 31 and 32, lines 54-67 and 19-31). Note that this composition is similar to the composition as disclosed in the specification on page 13, line 28-29. Therefore, since the reference discloses the same composition as disclosed in the specification, with the same ionic strength and pH, the composition described in Havelund et al. would inherently result in aggregate formations.

2. Claims 61-69 are rejected under 35 U.S.C. 102(e) as being anticipated by Norup et al.

The claims are drawn to water soluble aggregate of an insulin derivative having a lipophilic group and has a molecular weight larger than aldolase and comprise at lease 2 zinc ions per 6 moles of insulin derivative.

The reference teaches various insulin formulations that comprise insulin, phenolic compound such as cresol, glycerol, sodium chloride and varying amounts of zinc (see col. 4, lines 1-16 and 31-61). The pH of the composition is of the 7.2 when 20 mM of NaCl is present (see col. 4, lines 34-62). The composition utilizes insulin derivatives that include, B29-Nε-(N-lithocholyl -γ-glutamyl)-des(B30)-human insulin (see col. 3, lines 499-61). The difference between the prior art and the instant application is that the reference does not specifically teach aggregation of the insulin. However, since the reference discloses a composition with similar ionic strength and pH as the claimed composition, the composition disclosed by the reference would necessarily result in aggregate formations. Moreover, since the reference teaches pharmaceutical formulations that are

intended to be used in-vivo, the formations aggregates would have occurred after injections since the environment would have the ionic strength and pH necessary for aggregates to form. Note the claims state that the aggregates are "formed in an environment having an ionic strength and pH of the tissue **after** subcutaneous injections."

3. Claims 61-69 are rejected under 35 U.S.C. 102(b) as being unpatentable over Havelund et al. (WO 95/07931).

The claims are drawn to water soluble aggregate of an insulin derivative having a lipophilic group and has a molecular weight larger than aldolase and comprise at lease 2 zinc ions per 6 moles of insulin derivative.

The reference teach insulin composition comprising 600 nmol/ml of insulin, 7 mM of sodium phosphate buffer at pH 7.5, 10 mM sodium chloride, 16 mM phenol, 16 mM cresol, 2-3 Zn+2/hexamer and 1.6%(w/v) glycerol (see page 55-56). For insulin analogs, the reference teaches, as acknowledge by Applicants on page 10 of the specification, the use of NεB29-lithocholoyl-α-glutamyl des (B30) (see page 54, lines 13-25). Furthermore, the reference states that the parenteral administration may be performed by subcutaneous injection (see page 27, lines 8-10). Therefore, since the reference discloses the same composition as disclosed in the specification, with the same ionic strength and pH, the composition described in Havelund et al. would necessarily result in aggregate formations. Thus since all of the structural limitation of the compound are met and the same mode of administration is also disclosed, the aggregation of the compound, after injection, would be necessarily be achieved.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback , can normally be reached on (571) 272-0961. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

5/18/04

Anish Gupta
Patent Examiner